510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k113661

B. Purpose for Submission:

New Device

C. Measurand:

Methamphetamine

D. Type of Test:

Qualitative and Semi-Quantitative Enzyme Immunoassay

E. Applicant:

Lin-Zhi International, Inc.

F. Proprietary and Established Names:

LZI Methamphetamine Immunoassay

LZI Methamphetamine Drug of Abuse Calibrators

LZI Methamphetamine Drug of Abuse Controls

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LAF	Class II	21 CFR § 862.3610 Methamphetamine test system	Toxicology (91)
DLJ	Class II	21 CFR § 862.3200 Clinical toxicology calibrator	Toxicology (91)
LAS	Class I, Reserved	21 CFR § 862.3280 Clinical toxicology control material	Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The LZI Methamphetamine Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of d-methamphetamine in human urine, at the cutoff value of 500 ng/mL. The assay is designed for professional use with a number of automated chemistry analyzers.

   The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of specimen for confirmation by a confirmatory method such as GCMS or LCMS or (2) permitting laboratories to establish quality control procedures.

   The LZI Methamphetamine Drugs of Abuse (DAU) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the LZI Methamphetamine Enzyme Immunoassay at a cutoff value of 500 ng/mL.

   The LZI Methamphetamine Drugs of Abuse (DAU) Controls are for use as assayed quality control materials to monitor the precision of the LZI Methamphetamine Enzyme Immunoassay at a cutoff value of 500 ng/mL.

   The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Performance data was provided for Hitachi 717 analyzer. The assay can be used on a clinical chemistry analyzer capable of measuring absorbance at 340 nanometers.

I. Device Description:

The LZI Methamphetamine Enzyme Immunoassay is a kit comprised of two reagents,

separately packed, but sold together in one kit (R1 and R2).

Reagent	Description
R1	Contains mouse monoclonal anti-methamphetamine antibody, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide as a preservative.
R2	Contains d-methamphetamine labeled with glucose-6-phosphate dehydrogenase (G6PDH) in buffer with sodium azide as a preservative.

The LZI Methamphetamine Enzyme Immunoassay calibrators and controls designated for use at 500 ng/mL cutoff contain 0, 250, 375, 500, 625, 1,000, and 2,000 ng/mL of d-methamphetamine in human urine with less than 0.1% sodium azide as preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   LZI Amphetamines 500 Homogenous Enzyme Immunoassay
   LZI Amphetamines 500 Drugs of Abuse Calibrators
   LZI Amphetamines 500 Drugs of Abuse Controls

2. Predicate 510(k) number(s):

   k102210

3. Comparison with predicate:

Similarities and Differences – Test Device

Item	Candidate Device	Predicate Device
	LZI Methamphetamine Enzyme Immunoassay	LZI Amphetamines 500 Homogenous Enzyme Immunoassay (k102210)

Intended Use	The Methamphetamine Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of d-methamphetamine in human urine, at the cutoff value of 500 ng/mL. The assay is designed for professional use with a number of automated chemistry analyzers. The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of specimen for confirmation by a confirmatory method such as GCMS or LCMS or (2) permitting laboratories to establish quality control procedures. The Methamphetamine Drugs of Abuse (DAU) Calibrators are for use as calibrators in the qualitative and semi-quantitative calibration of the Methamphetamine Enzyme Immunoassay at a cutoff value of 500 ng/mL. The Methamphetamine Drugs of Abuse (DAU) Controls are for use as assayed quality control materials to monitor the precision of the Methamphetamine Enzyme Immunoassay at a cutoff value of 500 ng/mL. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.	Same
Analytes	d-methamphetamine	d-amphetamine and d-methamphetamine
Assay Type	Qualitative and Semi-Quantitative	Same
Cutoff value	500 ng/mL	Same
Sample	Urine	Same

Methodology	Enzyme Immunoassay (EIA)	Enzyme Linked Immunoassay(ELISA)
Analyzer	Clinical chemistry analyzer capable of measuring absorbance at 340 nanometers	Same
Detection Wavelength	340 nanometers	Same
Calibrators	Five Levels (0, 250, 500, 1000, and 2,000)	Same
Controls	Two Levels (375 and 625 ng/mL)	Same

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A, Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

The assay is an Enzyme Immunoassay (EIA) based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate-dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity. In the absence of drug in the sample, methamphetamine-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody would bind to free drug, the unbound methamphetamine-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Precision studies were conducted on the Hitachi 717 analyzer using samples containing methamphetamine. Studies were performed according to CLSI-EP5. Samples were prepared by spiking a negative human urine pool with d-methamphetamine at the following concentrations: zero drug (-100%), -75%, -50%, and -25% below the cutoff, cutoff, and +25%, +50%, +75%, and +100% above the cutoff. Samples were tested in 2 replicates per run, 2 runs per day for 22 days, total n=88. Samples concentrations were confirmed by GC/MS. Results of the studies are presented below:

Semi-Quantitative		Within Run		Total Precision	
Sample Concentration (ng/mL)	% of Cutoff	Number of Determinations	Immunoassay Result	Number of Determinations	Immunoassay Result
0	-100%	22	22 Negative	88	88 Negative
125	-75%	22	22 Negative	88	88 Negative
250	-50%	22	22 Negative	88	88 Negative
375	-25%	22	22 Negative	88	88 Negative
500	Cutoff	22	22 Positive	88	85 Positive 3 Negative
625	+25%	22	22 Positive	88	88 Positive
750	+50%	22	22 Positive	88	88 Positive
875	+75%	22	22 Positive	88	88 Positive
1000	+100%	22	22 Positive	88	88 Positive

Qualitative		Within Run		Total Precision	
Sample Concentration (ng/mL)	% of Cutoff	Number of Determinations	Immunoassay Result	Number of Determinations	Immunoassay Result
0	-100%	22	22 Negative	88	88 Negative
125	-75%	22	22 Negative	88	88 Negative
250	-50%	22	22 Negative	88	88 Negative
375	-25%	22	22 Negative	88	88 Negative
500	Cutoff	22	16 Positive 6 Negative	88	62 Positive 26 Negative
625	+25%	22	22 Positive	88	88 Positive
750	+50%	22	22 Positive	88	88 Positive
875	+75%	22	22 Positive	88	88 Positive
1000	+100%	22	22 Positive	88	88 Positive

b. Linearity/assay reportable range:

Linearity across the range was confirmed by serially diluting a spike urine pool containing d-methamphetamine to obtain the levels listed in the table below. Each sample was assayed in 10 replicates on the Hitachi 717 analyzer in semi-quantitative mode. The results were averaged and compared to the expected result and the percent recovery was calculated. Results are presented below:

Expected Value (ng/mL)	Observed Value (ng/mL)	% Recovery
0	0	
25	22.5	86.0
150	130.6	87.0
300	291.6	97.2
400	403.1	100.8
500	497.1	99.4
600	591.6	98.6
750	726.2	96.8
1000	966.6	96.7
1400	1345.1	96.1
2000	1971.4	98.6

Linear regression analysis of the results yielded the following:

$y = 0.9791x - 2.8289$, $R^2 = 0.9996$

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Calibrators and controls were previously cleared (k102210) under a different trade name. The calibrators and controls of this current submission and the predicate only differ in trade name. See k102210 for calibrators and controls traceability and stability information.

Labeling indicates to not use assay reagents, calibrators, or control materials beyond the indicated expiration dates on labeled vials.

d. Detection limit:

Performance at low drug concentrations in the semi-quantitative assay was characterized by determination of recovery (see section M1b above).

e. *Analytical specificity:*

Possible interference from endogenous compounds was evaluated using pooled urine samples spiked with d-methamphetamine at levels ±25% of the 500 ng/mL cutoff. Interference was evaluated on the Hitachi 717 analyzer. No positive or negative interference was observed when the following endogenous compounds were tested at the physiological levels indicated in the table:

Compound	Concentration (mg/dL)	-25% d-methamphetamine (375 ng/mL)	+25% d-methamphetamine (625 ng/mL)
Acetone	1000	Negative	Positive
Ascorbic Acid	500	Negative	Positive
Creatinine	500	Negative	Positive
Ethanol	1000	Negative	Positive
Galactose	10	Negative	Positive
γ-Globulin	500	Negative	Positive
Glucose	1500	Negative	Positive
Hemoglobin	100	Negative	Positive
Human Serum Albumin	500	Negative	Positive
Oxalic Acid	100	Negative	Positive
Riboflavin	2.5	Negative	Positive
Sodium Chloride	2000	Negative	Positive
Urea	2000	Negative	Positive

Possible interference from specific gravity was evaluated using urine samples containing d-methamphetamine at levels ±25% of the 500 ng/mL cutoff with specific gravities ranging from 1.002 to 1.030. No positive or negative interference due to specific gravity was observed.

To test for potential positive or negative interference from pH using urine samples containing d-methamphetamine at levels ±25% of the 500 ng/mL cutoff were evaluated at pH values of 3, 4, 5, 6, 7, 8, 9, 10, and 11. No positive or negative interference due to pH was observed.

Cross reactivity of various potential interfering structurally related drugs was tested by spiking a final concentration of up to 500,000 ng/mL of each substance into drug-free urine. Final concentrations of drug compounds tested were equivalent to the 500 ng/mL d-methamphetamine cutoff. Cross-reactivity was evaluated with the assay's calibrated dose-response curve. Results from these studies are summarized below:

Structurally Related Compounds	Target Concentration (ng/mL)	Response equivalent to cutoff (ng/mL)	% Cross Reactivity
d-Amphetamine	10,000	253.85	2.54%
l-Amphetamine	12,000	122.20	1.02%
Atomoxetine	500,000	129.60	0.03%
Benzphetamine	500,000	172.85	0.03%
d-Ephedrine	150,000	487.00	0.32%
d,l-Ephedrine	200,000	417.95	0.21%
l-Ephedrine	100,000	350.20	0.35%
Fenfluramine	4,000	433.30	10.83%
4-Fluoromethcathinone (Flephedrone; 4-MC)	200,000	311.05	0.16%
3-Hydroxy-Tyramine	500,000	250.55	0.04%
Isoxsuprine	500,000	147.85	0.03%
Mephentermine	25,000	107.50	0.43%
l-Methamphetamine	5,000	486.45	9.73%
para-Methoxyamphetamine (PMA)	400	12.75	3.19%
para-Methoxymethylamphetamine (PMMA)	500	374.70	74.94%
Methylenedioxyamphetamine (MDA)	1,400	28.60	2.04%
Methylenedioxyethylamphetamine (MDEA)	10,000	350.15	3.50%
Methylenedioxymethylamphetamine (MDMA)	1,000	389.10	38.91%
4-Methylmethcathinone (Mephedrone; 4-MMC; PMMC)	100,000	393.40	0.39%
Phendimetrazine	150,000	300.35	0.20%
Phenethylamine	25,000	294.55	1.18%
Phenmetrazine	40,000	418.45	1.05%
Phentermine	20,000	40.20	0.20%
phenylephrine	300,000	467.60	0.16%
d,l-Phenylpropanolamine	150,000	92.30	0.06%
d-Pseudoephedrine	112,500	441.25	0.39%
l-Pseudoehedrine	200,000	178.25	0.09%
Tranylcypromine	50,000	286.70	0.57%
Tyramine	400,000	350.05	0.09%

Cross-reactivity of non-structurally related compounds was evaluated by testing compounds spiked into urine samples containing d-methamphetamine at levels ±25% of the 500 ng/mL cutoff. Non-structurally related compounds were tested at the concentration levels indicated in the table below. Cross-reactivity was evaluated with the assay's calibrated dose-response curve. Results from these studies are summarized below:

Non-Structurally Related Compounds	Target Concentration (ng/mL)	Response equivalent to cutoff (ng/mL)	% Cross Reactivity
Acetaminophen	400,000	2.9	0.001
Acetylsalicylic acid	500,000	7.4	0.001
Amobarbital	250,000	72.3	0.029
Benzoylecgonine	250,000	75.2	0.030
Bromopheniramine	250,000	100.3	0.040
Burpropion	100,000	90.6	0.091
Buspiron	125,000	86.1	0.069
Caffeine	500,000	9.1	0.002
Chlorpheniramine	250,000	47.2	0.019
Chlorpromazine	250,000	99.6	0.040
Codeine	250,000	79.5	0.032
Dextromethorphan	500,000	11.4	0.002
Doxepine	200,000	11.5	0.006
Meperidine	250,000	79.6	0.032
Methadone	250,000	96.5	0.039
Methapyrilene	100,000	89.8	0.090
Methaqualone	250,000	81.7	0.033
Morphine	500,000	8.5	0.002
Oxazepam	250,000	85.5	0.034
Phencyclidine	500,000	101.1	0.020
Phenobarbital	250,000	74.5	0.030
Phenothiazine	50,000	24.5	0.049
Procainamide	30,000	105.3	0.351
Promethazine	250,000	44.6	0.018
Propoxyphene	250,000	76.8	0.031
Propranolol	250,000	85.2	0.034
Ranitidine	5,000	178.0	3.559
Scopolamine	250,000	77.5	0.031
Secobarbital	250,000	74.9	0.030
Sertraline	125,000	106.9	0.085
Thioridazine	250,000	99.8	0.040
Trazodone	50,000	81.8	0.164
Trifluoperazine	125,000	67.9	0.054
Trifluopromazine	125,000	65.2	0.052
Valproic Acid	500,000	14.8	0.003

f. Assay cut-off:

There is a 500 ng/mL cutoff concentration claimed for this assay. See section M1a above for performance data around the cutoff.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor conducted a method comparison study to evaluate the performance of the device for detection of d-methamphetamine by testing 95 unaltered samples (48 negative and 47 positive samples) on the Hitachi 717 analyzer. Results were compared to results obtained with GC/MS or LC/MS. Studies were conducted in semi-quantitative and qualitative modes. Equivalent results were obtained for both modes. Study results are summarized below:

Method Comparison Results (500 ng/mL Cutoff)					
Candidate Device Results	Negative	< 50% of the cutoff (1-250 ng/mL)	Near Negative Cutoff (250-500 ng/mL)	Near Positive Cutoff (500-750 ng/mL)	High Positive (>750 ng/mL)
Positive (47 samples)	0	0	0	9	37
Negative (48 samples)	20	16	12	1	0

Discordant Results	
Candidate Device Result	GC/MS or LC/MS Result
Negative	654 ng/mL

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.